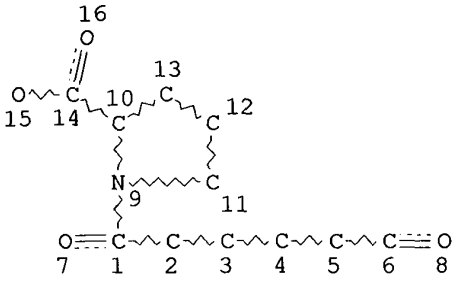
=> d que
L13 STR



NODE ATTRIBUTES:
CONNECT IS E1 RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L16 26 SEA FILE=REGISTRY SSS FUL L13
L17 11 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

=> d ibib abs hitstr l17 1-11

L17 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:42246 HCAPLUS
TITLE: Preparation of amino acid derivatives as prolyl oligopeptidase inhibitors
INVENTOR(S): Gynther, Jukka; Maennistoe, Pekka; Wallen, Erik; Christiaans, Johannes; Forsberg, Markus; Poso, Antti; Venaelaeinen, Jarkko; Helkala, Elina
PATENT ASSIGNEE(S): Orion Corporation, Finland
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004468	A1	20030116	WO 2002-FI607	20020704

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

Get this.

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FI 2001-1466 A 20010704

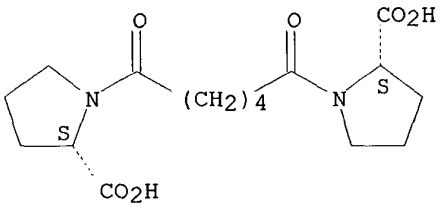
AB Amino acid derivs. G-CO-Q-CO-aa-A [aa is a residue of an .alpha.-amino acid; Q is a covalent bond, (un)substituted (cyclo)alk(en)ylene, or arylene; A is (un)substituted alk(en)yl, carbo- or heterocyclyl; G = aa'-E (aa' is an .alpha.-amino acid residue and E is a group defined similarly to A) or an amino functionality contg. a heterocyclic ring] or their pharmaceutically-acceptable salts were prepd. for use as prolyl oligopeptide inhibitors, e.g., for the treatment of Alzheimer's disease. Thus, glutaric acid bis(L-prolylpyrrolidine) amide was prepd. via coupling reactions and showed IC50 = 48 nM for inhibition of pig prolyl oligopeptidase.

IT **155885-27-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid derivs. as prolyl oligopeptidase inhibitors)

RN 155885-27-1 HCAPLUS

CN L-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:650987 HCAPLUS

DOCUMENT NUMBER: 137:325613

TITLE: Dicarboxylic Acid bis(L-Prolyl-pyrrolidine) Amides as Prolyl Oligopeptidase Inhibitors

AUTHOR(S): Wallen, Erik A. A.; Christiaans, Johannes A. M.; Forsberg, Markus M.; Venaelaeinen, Jarkko I.; Maennistoe, Pekka T.; Gynther, Jukka

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kuopio, Kuopio, FIN-70211, Finland

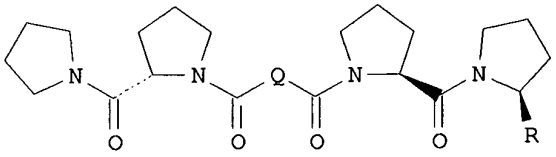
SOURCE: Journal of Medicinal Chemistry (2002), 45(20), 4581-4584
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

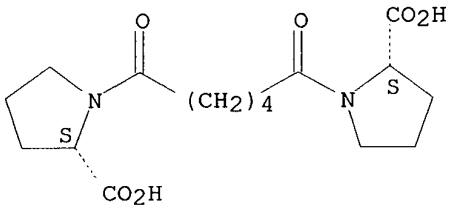
AB New dicarboxylic acid bis(L-prolyl-pyrrolidine) amides I [Q = (CH2)n, n = 2-4 with R = H; Q = CH2C(Me)2CH2, R = H; Q = o-, m-, p-phenylene with R = H; Q = m-phenylene with R = CHO, CN, COCH2OH] were synthesized, and their inhibitory activity against prolyl oligopeptidase from pig brain was tested in vitro. As compared with prolyl oligopeptidase inhibitors described earlier, I has in common an L-prolyl-pyrrolidine moiety, but the typical lipophilic acyl end group is replaced by another L-prolyl-pyrrolidine moiety connected sym. with a short dicarboxylic acid linker. I is a new type of peptidomimetic prolyl oligopeptidase inhibitor.

IT **155885-27-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of dicarboxylic acid bis(prolyl-pyrrolidine)amides as inhibitors of prolyl oligopeptidase)

RN 155885-27-1 HCAPLUS

CN L-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:362347 HCAPLUS

DOCUMENT NUMBER: 137:320267

TITLE: Targeted pharmacological depletion of serum amyloid P component for treatment of human amyloidosis

AUTHOR(S): Pepys, M. B.; Herbert, J.; Hutchinson, W. L.; Tennent, G. A.; Lachmann, H. J.; Gallimore, J. R.; Lovat, L. B.; Bartfai, T.; Alanine, A.; Hertel, C.; Hoffmann, T.; Jakob-Roetne, R.; Norcross, R. D.; Kemp, J. A.; Yamamura, K.; Suzuki, M.; Taylor, G. W.; Murray, S.; Thompson, D.; Purvis, A.; Kolstoe, S.; Wood, S. P.; Hawkins, P. N.

CORPORATE SOURCE: Centre for Amyloidosis and Acute Phase Proteins, Department of Medicine, Royal Free and University College Medical School, London, NW3 2PF, UK

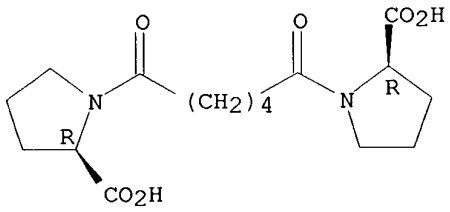
SOURCE: Nature (London, United Kingdom) (2002), 417(6886), 254-259
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The normal plasma protein serum amyloid P component (SAP) binds to fibrils in all types of amyloid deposits, and contributes to the pathogenesis of amyloidosis. In order to intervene in this process we have developed a drug, R-1-[6-[R-2-carboxy-pyrrolidin-1-yl]-6-oxo-hexanoyl]pyrrolidine-2-carboxylic acid, that is a competitive inhibitor of SAP binding to amyloid fibrils. This palindromic compd. also crosslinks and dimerizes SAP mols., leading to their very rapid clearance by the liver, and thus produces a marked depletion of circulating human SAP. This mechanism of drug action potently removes SAP from human amyloid deposits in the tissues and may provide a new therapeutic approach to both systemic amyloidosis and diseases assocd. with local amyloid, including Alzheimer's disease and type 2 diabetes.

IT **224624-80-0**, Ro 63-8695
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CPHPC; targeted pharmacol. depletion of serum amyloid P component for treatment of human amyloidosis)

RN 224624-80-0 HCAPLUS
CN D-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Claim 20.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:343650 HCAPLUS
DOCUMENT NUMBER: 130:352548
TITLE: Synthesis of D-proline derivatives for treatment of amyloidosis
INVENTOR(S): Hertel, Cornelia; Hoffmann, Torsten; Jakob-Roetne, Roland; Norcross, Roger David
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 77 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 915088	A1	19990512	EP 1998-119986	19981022
EP 915088	B1	20020918		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 224366	E	20021015	AT 1998-119986	19981022
US 6103910	A	20000815	US 1998-179652	19981027
ZA 9809889	A	19990430	ZA 1998-9889	19981029
AU 9889599	A1	19990520	AU 1998-89599	19981029
AU 750734	B2	20020725		
JP 11209343	A2	19990803	JP 1998-307719	19981029
JP 3048558	B2	20000605		
NO 9805059	A	19990503	NO 1998-5059	19981030
CN 1217327	A	19990526	CN 1998-123674	19981030
BR 9804378	A	20000613	BR 1998-4378	19981030
SG 74094	A1	20000718	SG 1998-4381	19981030
US 6262089	B1	20010717	US 2000-505375	20000216
US 6512001	B1	20030128	US 2000-636076	20000810

PRIORITY APPLN. INFO.:
EP 1997-119031 A 19971031
EP 1998-113851 A 19980724
US 1998-179652 A3 19981027
US 2000-505375 A3 20000216

OTHER SOURCE(S): MARPAT 130:352548

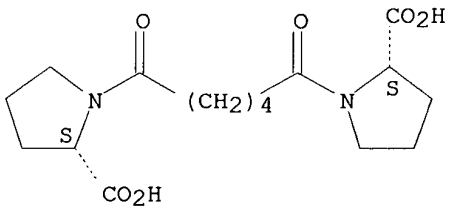
AB D-Proline derivs. R-X-CO-D-Pro-OH [R = SH, benzyl, Ph, hydroxy- or alkoxy-Ph, or D-Pro-OH; X = (CH2)n, (CH2)nCHR2, (CH2)nOCH2, NHCH2, benzyl, CH:CR2, CH(OH)CH2, thiazol-2,5-diyl (n = 0-3, R2 = alkyl, alkoxy, benzyl)] and related di-D-proline derivs. linked at X by SS, (CH2)n, O, NH, NR2, phenylene, etc., as well as corresponding 4-halo and 3,4-didehydro derivs., were prepd. for the treatment of amyloidosis. Thus, (R)-1-[(S)-3-[(S)-3-[(R)-2-carboxypyrrolidin-1-yl]-2-methyl-3-oxopropyl-dithio]-2-methyl-propionyl]pyrrolidine-2-carboxylic acid was prepd. by acylation of D-proline tert-Bu ester with AcSCH2CHMeCOCl, followed by ester cleavage and disulfide coupling.

IT **155885-27-1P 224624-80-0P 224625-59-6P 224625-60-9P 224625-61-0P 224625-62-1P 224625-63-2P 224625-64-3P 224625-65-4P 224625-67-6P 224625-68-7P 224625-70-1P 224625-71-2P 224625-89-2P 224625-92-7P 224625-94-9P 224626-00-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of D-proline derivs. for treatment of amyloidosis)

RN 155885-27-1 HCAPLUS

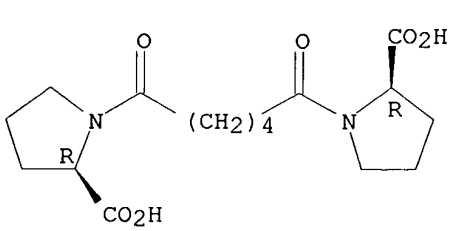
CN L-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



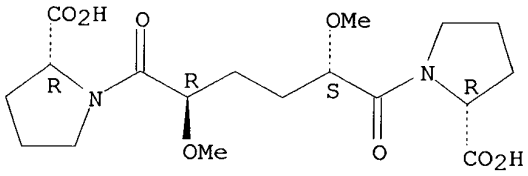
RN 224624-80-0 HCAPLUS
CN D-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



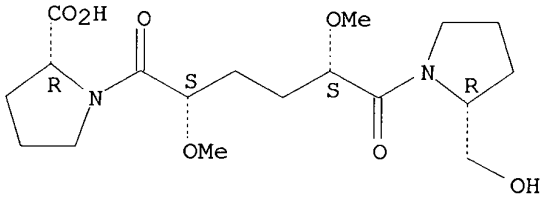
RN 224625-59-6 HCAPLUS
CN D-Proline, 1,1'-[(2R,5S)-2,5-dimethoxy-1,6-dioxo-1,6-hexanediyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



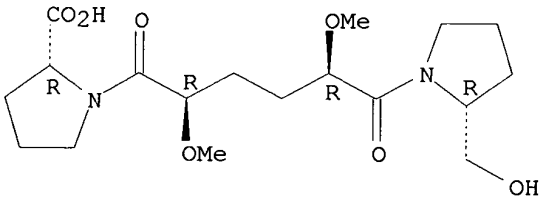
RN 224625-60-9 HCAPLUS
CN D-Proline, 1-[(2S,5S)-6-[(2R)-2-(hydroxymethyl)-1-pyrrolidinyl]-2,5-dimethoxy-1,6-dioxohexyl]- (9CI) (CA INDEX NAME)

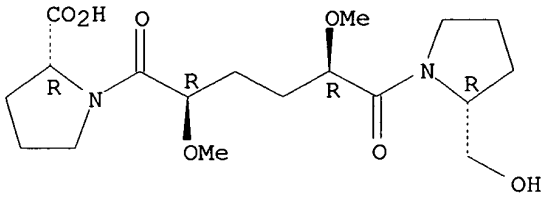
Absolute stereochemistry.



RN 224625-61-0 HCAPLUS
CN D-Proline, 1-[(2R,5R)-6-[(2R)-2-(hydroxymethyl)-1-pyrrolidinyl]-2,5-dimethoxy-1,6-dioxohexyl]- (9CI) (CA INDEX NAME)

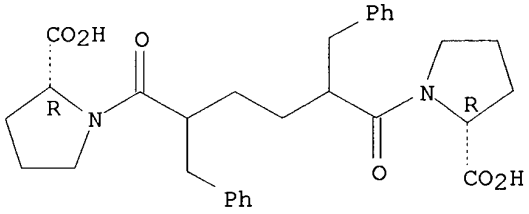
Absolute stereochemistry.





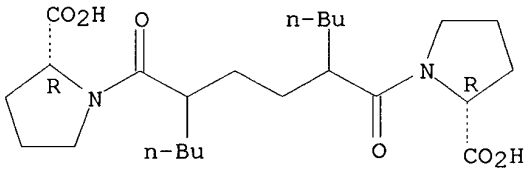
RN 224625-62-1 HCAPLUS
CN D-Proline, 1,1'-[1,6-dioxo-2,5-bis(phenylmethyl)-1,6-hexanediyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



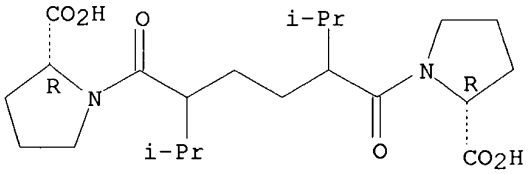
RN 224625-63-2 HCAPLUS
CN D-Proline, 1,1'-(2,5-dibutyl-1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



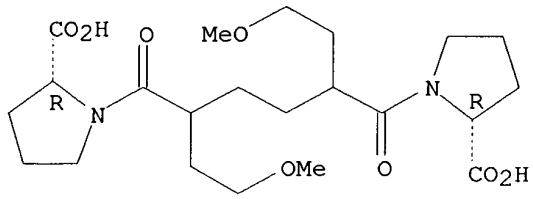
RN 224625-64-3 HCAPLUS
CN D-Proline, 1,1'-[2,5-bis(1-methylethyl)-1,6-dioxo-1,6-hexanediyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



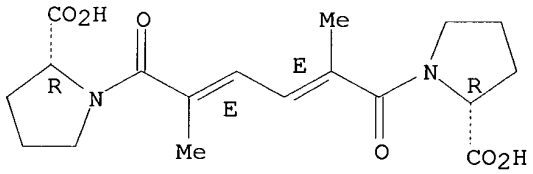
RN 224625-65-4 HCAPLUS
CN D-Proline, 1,1'-[2,5-bis(2-methoxyethyl)-1,6-dioxo-1,6-hexanediyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



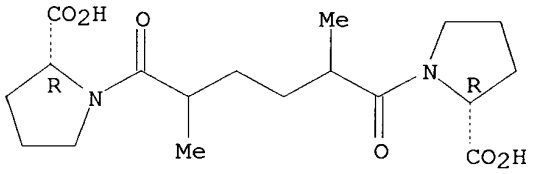
RN 224625-67-6 HCAPLUS
CN D-Proline, 1,1'-[(2E,4E)-2,5-dimethyl-1,6-dioxo-2,4-hexadiene-1,6-diyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



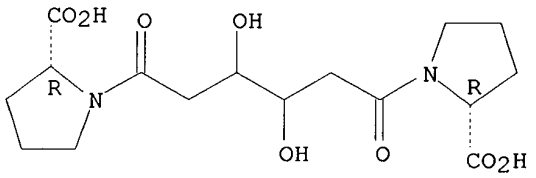
RN 224625-68-7 HCAPLUS
CN D-Proline, 1,1'-(2,5-dimethyl-1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 224625-70-1 HCAPLUS
CN D-Proline, 1,1'-(3,4-dihydroxy-1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

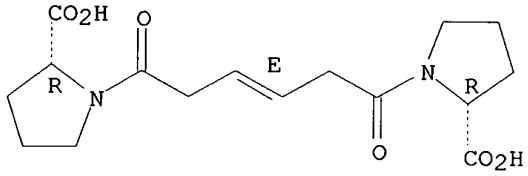
Absolute stereochemistry.



RN 224625-71-2 HCAPLUS

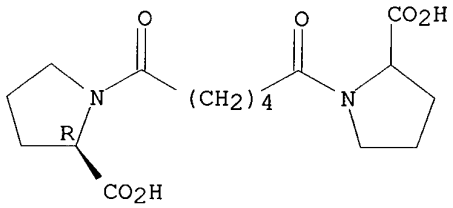
CN D-Proline, 1,1'-[(3E)-1,6-dioxo-3-hexene-1,6-diyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

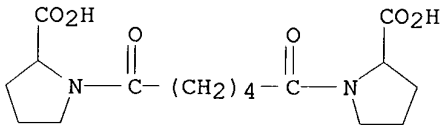


RN 224625-89-2 HCAPLUS
CN Proline, 1-[6-[(2R)-2-carboxy-1-pyrrolidinyl]-1,6-dioxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

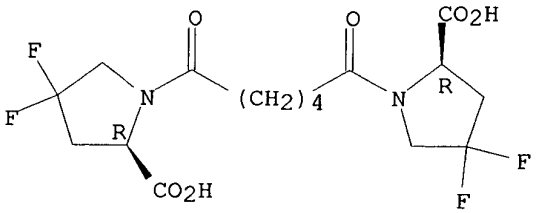


RN 224625-92-7 HCAPLUS
CN Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)



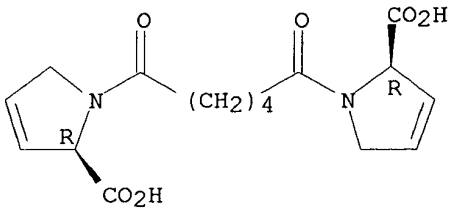
RN 224625-94-9 HCAPLUS
CN D-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis[4,4-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 224626-00-0 HCAPLUS
CN 1H-Pyrrole-2-carboxylic acid, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis[2,5-dihydro-, (2R,2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

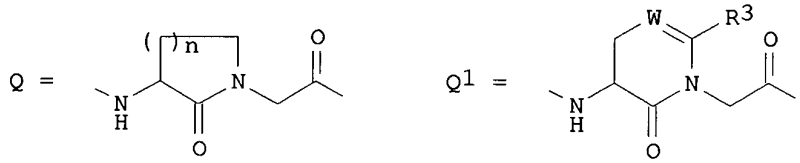


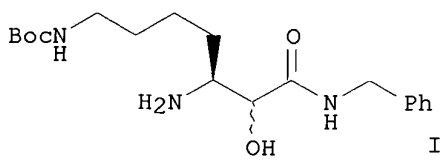
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:745086 HCAPLUS
DOCUMENT NUMBER: 130:4091
TITLE: Preparation of backbone-cyclized peptide derivatives as serine protease and thrombin inhibitors
INVENTOR(S): Adang, Anton Egbert Peter
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850420	A1	19981112	WO 1998-EP2587	19980428
W: AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876520	A1	19981127	AU 1998-76520	19980428
AU 729910	B2	20010215		
EP 979240	A1	20000216	EP 1998-924265	19980428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9809342	A	20000704	BR 1998-9342	19980428
JP 2001524117	T2	20011127	JP 1998-547715	19980428
RU 2183642	C2	20020620	RU 1999-125967	19980428
ZA 9803629	A	19981104	ZA 1998-3629	19980429
NO 9905316	A	19991101	NO 1999-5316	19991101

PRIORITY APPLN. INFO.: EP 1997-201286 A 19970502
WO 1998-EP2587 W 19980428
OTHER SOURCE(S): MARPAT 130:4091
GI





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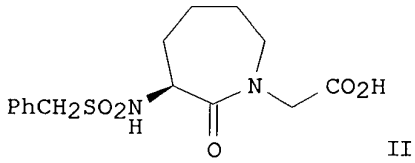
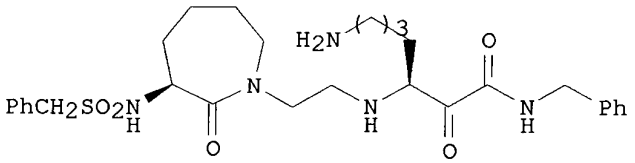


II



III

AB The invention relates peptide derivs. R1SO2-B-X-Z-CO-Y [B = bond, amino acid NHCH[(CH2)pCO2H]CO or ester deriv. thereof, Gly, D-1-perhydroiosquinolinecarboxylic acid (D-1-Piq), D-3-Piq, D-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid (D-1-Tiq), D-3-Tiq, D-aminotetralincarboxylic acid, aminoindanecarboxylic acid, L- or D-amino acid contg. hydrophobic, basic, or neutral side chain; X = amino acid contg. hydrophobic side chain, Gln, Ser, Thr, 2-aminoisobutyric acid, NR2CH2CO, Q, Q1, cyclic amino acid optionally contg. addnl. heteroatom N, O or S, (un)substituted with C1-6 alkyl, C1-6 alkoxy, PhCH2O, oxo; Z = Lys, 4-aminocyclohexylglycine; Y = (un)substituted NHC1-6 alkylene-Ph, OR4, NR5R6; W = CH, N; R1 = R2O2C(CHR2)m, R2NH(CHR2)m, (un)substituted C1-12 alkyl, C2-12 alkenyl, C6-14 aryl, C7-15 aralkyl, C8-16 aralkenyl; each R2 = independently H, C1-12 alkyl, C3-8 cycloalkyl, (un)substituted C6-14 aryl or C7-15 aralkyl; R3 = H, C1-6alkyl, Ph optionally substituted with OH, C1-6 alkoxy, CO2H, CO2-C1-6 alkyl, CONH2, halo; R4 = H, C2-6 alkyl, CH2Ph; R5, R6 = independently H, C1-6 alkoxy, (un)substituted C1-6 alkyl; R5R6 = CH2CH2VCH2CH2; V = O, S, SO2; m = 1-3; n = 2-4; p = 1-3]. The compds. of the invention have anticoagulant activity and can be used in treating or preventing thrombin-related diseases. Thus, coupling of homologated Lys deriv. I (prepd. in 6 steps from Cbz-Lys(Boc)-OH, NaCN, and benzylamine) with backbone-cyclized dipeptide deriv. II (prepd. in 4 steps from L-.alpha.-amino-.epsilon.-caprolactam, Me bromoacetate, and benzylsulfonyl chloride), followed by oxidn. and deprotection gave desired title compd. III. III inhibited factor Xa with IC50 = 0.64 .mu.M.

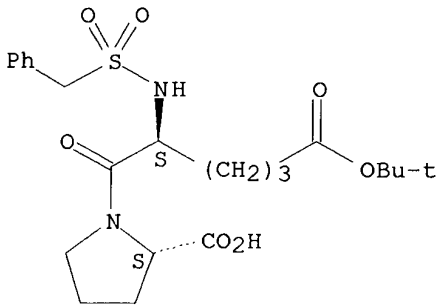
IT **215791-99-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of backbone-cyclized peptide derivs. as serine protease

inhibitors)
RN 215791-99-4 HCAPLUS
CN L-Proline, 6-(1,1-dimethylethoxy)-6-oxo-N-[(phenylmethyl)sulfonyl]-L-norleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



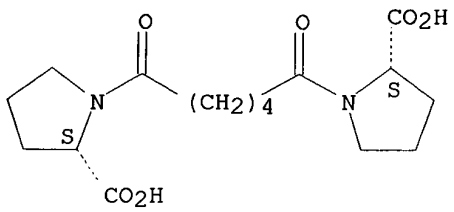
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:497803 HCAPLUS
DOCUMENT NUMBER: 121:97803
TITLE: Electrolytic capacitor solution containing amide-containing dicarboxylic acid
INVENTOR(S): Ue, Makoto; Takeda, Masayuki; Sato, Tomohiro
PATENT ASSIGNEE(S): Mitsubishi Petrochemical Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06061099	A2	19940304	JP 1992-208759	19920805

PRIORITY APPLN. INFO.: JP 1992-208759 19920805
OTHER SOURCE(S): MARPAT 121:97803
GI For diagram(s), see printed CA Issue.
AB The soln. contains amide-contg. dicarboxylic acids or their salts. The dicarboxylic acids may be (HO2CYNRCO)2X or I (X = dicarboxylic acid residue; Y = amino acid residue; Z = alkyl, H; Z = heterocyclic amino acid residue). The soln. showed good low-temp. property.
IT **155885-27-1**
RL: DEV (Device component use); USES (Uses)
(electrolytic capacitor soln. contg., with good low-temp. property)
RN 155885-27-1 HCAPLUS
CN L-Proline, 1,1'-(1,6-dioxo-1,6-hexanediyl)bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:405725 HCAPLUS
DOCUMENT NUMBER: 113:5725
TITLE: Preparation of succinylacetone derivatives and analogs as immunosuppressive agents
INVENTOR(S): Nitecki, Danute E.; Moreland, Margaret; Aldwin, Lois; Levenson, Corey H.; Braude, Irwin; Mark, David F.
PATENT ASSIGNEE(S): Cetus Corp., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9000049	A2	19900111	WO 1989-US2762	19890623
WO 9000049	A3	19900308		
W: AU, DK, FI, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4895872	A	19900123	US 1989-324360	19890315
AU 9047599	A1	19900123	AU 1990-47599	19890623
US 5173482	A	19921222	US 1990-624078	19901206
US 5216005	A	19930601	US 1990-623095	19901206
US 5252603	A	19931012	US 1990-623096	19901206

PRIORITY APPLN. INFO.: US 1988-212957 19880629
US 1989-324360 19890315
WO 1989-US2762 19890623
US 1989-434870 19891113

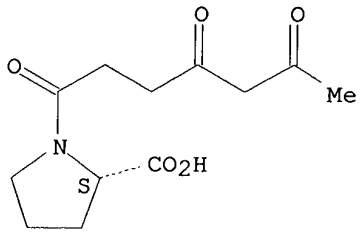
OTHER SOURCE(S): MARPAT 113:5725

AB RCOCR1R2CO(CH2)nR3 [I; n = 1-6; R = Me, CF3, CHO, COMe, CO2R4; R4 = H, alkyl; R1, R2 = H, F, Me, CH2, CH2CO2R4; R3 = H, CO2R, P(O)(OR4)2, CONHR4, tetrazolyl], useful for the treatment of autoimmune diseases and graft vs. host rejection, are prepd. Thus, treatment of a soln. of MeCOCH2COCH2CH2COR (II; R = OH) and 1-hydroxy-1-nitrobenzene-4-sulfuric acid in DMF with DCC followed by proline gave II (R = Pro-OH) which was converted into the p-nitrophenyl active ester by treatment with p-O2NC6H4OH and DCC in CHCl3 and then condensed with PEG-4000-NH2 (III) (PEG = polyethylene glycol) to give, after chromatog. on a Sephadex G-50 column, MeCOCH2COCH2CH2CO-Pro-NH-PEG (IV). IV in vitro inhibited the prodn. of interleukin-2 and interferon-.gamma. in human lymphocytes by 98.9 and 96.9% resp. vs. III 20.6 and 20.1%, resp. Addnl. 10 I were prepd.

IT **127528-59-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)

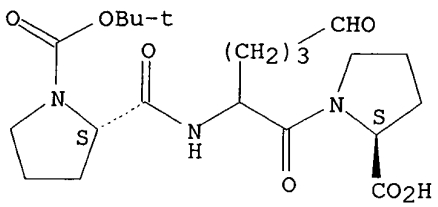
(prepn. and condensation of, with aminopolyethylene glycol)
RN 127528-59-0 HCAPLUS
CN L-Proline, 1-(1,4,6-trioxoheptyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



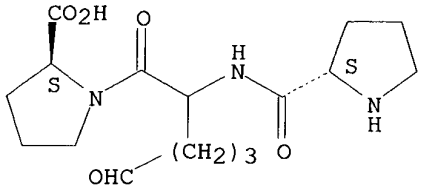
L17 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:478570 HCAPLUS
DOCUMENT NUMBER: 111:78570
TITLE: Allysine peptides and derivatives
AUTHOR(S): Doelz, R.; Heidemann, E.
CORPORATE SOURCE: Dep. Protein Leather, Inst. Macromol. Chem., Darmstadt, Fed. Rep. Ger.
SOURCE: International Journal of Peptide & Protein Research (1988), 32(4), 307-20
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:78570
AB Allysine, OCH(CH2)3CH(NH2)CO2H, which is synthesized enzymically in vivo starting from lysine, is a very important crosslink precursor in proteins. The chem. synthesis of allysine derivs. starting from 3,4-dihydro-2H-pyran is described. Two independent synthetic routes for the prepn. of allysine peptides and derivs. are presented. The synthesized compds. are characterized by spectroscopic methods including 13C NMR. The reactivity of the aldehyde function is shown to be extremely high. An unexpected nucleophilic attack of the allysine amide nitrogen at the aldehyde group is described. This ring closure reaction is not expected to occur in native collagen; however, denatured peptides contg. allysine may react similarly to the model peptides.
IT **121895-31-6P 121895-32-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of, dehydropipecolic acid deriv. from)
RN 121895-31-6 HCAPLUS
CN L-Proline, 1-[N-[1-[(1,1-dimethylethoxy)carbonyl]-L-prolyl]-6-oxonorleucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 121895-32-7 HCAPLUS
CN L-Proline, 1-(6-oxo-N-L-prolylnorleucyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

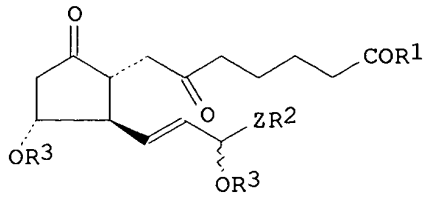


L17 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:617356 HCAPLUS
DOCUMENT NUMBER: 107:217356
TITLE: Process for the preparation of 6-prostaglandin E1 derivatives as cytoprotective agents
INVENTOR(S): Wakatsuka, Hirohisa; Okegawa, Tadao; Arai, Yoshinobu
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 232126	A2	19870812	EP 1987-300755	19870128
EP 232126	A3	19871125		
EP 232126	B1	19900816		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 62277352	A2	19871202	JP 1987-3315	19870112
US 4783480	A	19881108	US 1987-7657	19870128
AT 55598	E	19900915	AT 1987-300755	19870128
ES 2029830	T3	19921001	ES 1987-300755	19870128

PRIORITY APPLN. INFO.: JP 1986-16722 19860130
EP 1987-300755 19870128

OTHER SOURCE(S): CASREACT 107:217356
GI



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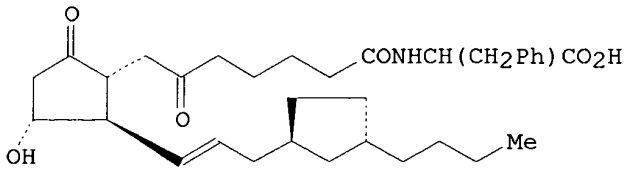

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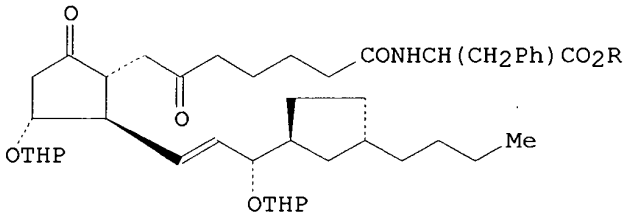


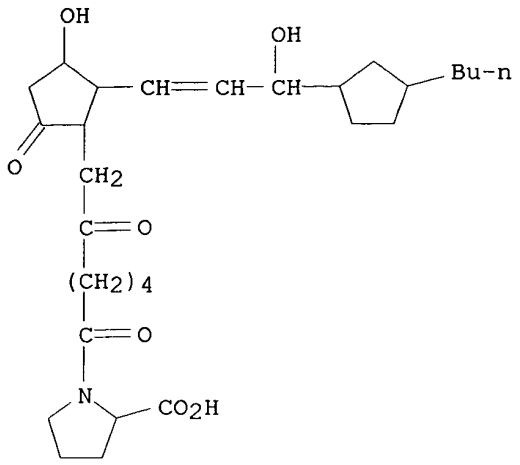
II

AB The title compds. I [R1 = amino acid or amino alc. residue attached to the CO group by its amino group; R2 = alkyl, (un)substituted cycloalkyl, Ph, PhO; R3 = H; Z = single bond, alkylene group; when Z is single bond, R2 .noteq. PhO], useful as cytoprotective agents, were prepd. via (a) amidation of carboxylic acid I (R1 = H; other Markush variables = as given above) with an amino acid or an amino alc.; (b) hydrolysis or alcoholysis of I (R3 = tetrahydropyran-2-yl, tetrahydro-2-furanyl, 1-ethoxyethyl; other Markush variables = as defined above); (c) deprotection of the carboxy-protecting group in I (as given above, with R1 as an amino acid residue having a protected carboxy group) by Zn. L-Phenylalanine 2,2,2-trichloroethyl ester.HBr was condensed with (13E)-(11.alpha.,15.alpha.,16S,18S)-6,9-dioxo-11,15-bis(tetrahydropyran-2-yloxy)-16,18-ethano-20-ethylprost-13-enoic acid to give the corresponding amide II (THF = tetrahydropyran-2-yl, R = CH2CCl3), which was then deprotected with Zn in AcOH at room temp. to give prostaglandin deriv. IIa. When injected i.p., IIa exhibited a min. ED of <10 .mu.g/kg against CCl4-induced liver damage in rats. An injectable compn. (for 100 ampules) contg. 2 mg N-[(13E)-(11.alpha.,15.alpha.,16S,18S)-6,9-dioxo-11,15-dihydroxy-16,18-ethano-20-ethylprost-13-en-1-oyl]-L-leucine (III) and 6 g maltose in 40 mL H2O was prepd.

IT **111111-05-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as cytoprotective agent)

RN 111111-05-8 HCAPLUS

CN L-Proline, 1-[7-[2-[3-(3-butylcyclopentyl)-3-hydroxy-1-propenyl]-3-hydroxy-5-oxocyclopentyl]-1,6-dioxoheptyl]-, [1R-[1.alpha.,2.beta.[1E,3S*(1S*,3S*)],4.alpha.]]- (9CI) (CA INDEX NAME)

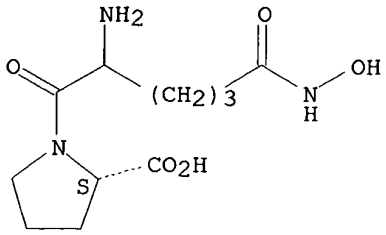


L17 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1984:239 HCAPLUS
DOCUMENT NUMBER: 100:239
TITLE: Dipeptide-hydroxamates are good inhibitors of the angiotensin I-converting enzyme
AUTHOR(S): Harris, Robert B.; Strong, Peter D. M.; Wilson, Irwin B.
CORPORATE SOURCE: Dep. Chem., Univ. Colorado, Boulder, CO, 80309, USA
SOURCE: Biochemical and Biophysical Research Communications (1983), 116(2), 394-9
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibition consts. (Ki) and modes of inhibition have been detd. for a series of dipeptide-hydroxamate compds. with bovine lung parenchyma angiotensin I-converting enzyme (E.C. 3.4.15.1) [9015-82-1]. The hydroxamido function was borne by aspartic, glutamic, or aminoadipic acid and extended by 2, 3 or 4 bond lengths from the proline amide bond. L-glu(NHOH)-L-pro [88070-87-5] (Ki = 3.4 .mu.M) and D,L-aminoadipicyl (NHOH)-L-pro [**88070-88-6**] (Ki = 1.2 .mu.M) were the best competitive inhibitors of the hydrolysis of benzoyl-gly-his-gly but were not effective as affinity ligands for purifn. of the enzyme.

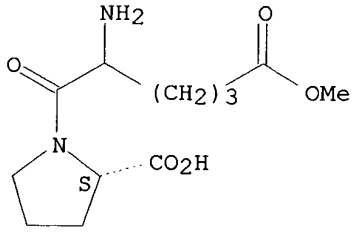
IT **88070-88-6**
RL: BIOL (Biological study)
(as angiotensin I-converting enzyme inhibitor, structure in relation to)
RN 88070-88-6 HCAPLUS
CN L-Proline, 1-[N6-hydroxy-6-oxolysyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



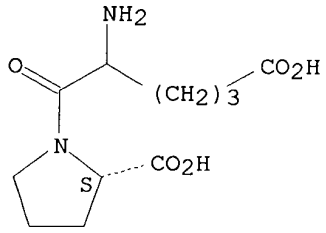
IT **88070-86-4P 88089-14-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and angiotensin I-converting enzyme inhibition by, structure in relation to)
RN 88070-86-4 HCAPLUS
CN L-Proline, 1-(6-methoxy-6-oxonorleucyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 88089-14-9 HCAPLUS
CN L-Proline, 1-(5-carboxynorvalyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:18091 HCAPLUS
DOCUMENT NUMBER: 88:18091
TITLE: Design of potent competitive inhibitors of angiotensin-converting enzyme. Carboxyalkanoyl and mercaptoalkanoyl amino acids
AUTHOR(S): Cushman, D. W.; Cheung, H. S.; Sabo, E. F.; Ondetti, M. A.
CORPORATE SOURCE: Squibb Inst. Med. Res., Princeton, NJ, USA

SOURCE: Biochemistry (1977), 16(25), 5484-91
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A hypothetical model of the active site of angiotensin-coverting enzyme (I) was utilized to guide the design and synthesis of specific inhibitors. By analogy to bovine carboxypeptidase A, the active site of I was proposed to contain 3 important groups that participate in binding of peptide substrates: a carboxyl-binding group, a group with affinity for the C-terminal peptide bond, and a tightly bound Zn2+ that could coordinate with the carbonyl of the penultimate (scissiie) peptide bond. According to the model, a succinyl amino acid could interact with each of these binding groups via its amino acid carboxyl, amide bond, and succinyl carboxyl, resp., and thus act as a specific competitive inhibitor of the enzyme. Succinyl-L-proline was such an inhibitor (I50 = 330 .mu.M), and attempts to optimize its interaction with the active site of the enzyme as proposed in the model led to the synthesis of D-2-methylsuccinyl-L-proline (R,S) (Ki = 2.5 .mu.M), and D-2-methylglutaryl-L-proline (R,S) (Ki = 0.8 .mu.M). Replacement of the succinyl carboxyl group of these compds. by a SH group led to a series of extremely potent competitive inhibitors of I, including 3-mercaptopropranoyl-L-proline (SQ 13,863, Ki = 0.012 .mu.M) and D-3-mercapto-2-methylpropranoyl-L-proline (S,S) (SQ 14,225, Ki = 0.0017 .mu.M). These compds. are also potent orally active inhibitors of I and have great potential as antihypertensive agents.

IT **65134-71-6**
RL: BIOL (Biological study)
(angiotensin I-converting enzyme inhibition by)

RN 65134-71-6 HCAPLUS

CN 1-Pyrrolidinehexanoic acid, 2-carboxy-.epsilon.-oxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.